UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

IV

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/176,664	10/21/98	SALKOFF	L 018512-00012

020350 HM12/0103
TOWNSEND AND TOWNSEND AND CREW
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO CA 94111-3834

EXAMINER	
BASI, N	
ART UNIT	**PAPER NUMBER**
1646	17

DATE MAILED: 01/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/176,664	Applicant(s) Salkoff et al
	Examiner Nirmal. S. Basi	Group Art Unit 1646

☒ Responsive to communication(s) filed on *Oct 16, 2000* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-48* is/are pending in the application.

Of the above, claim(s) *17-25 and 28-44* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-16, 26, 27, and 45-48* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The amendments filed 10/16/00 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action (4/10/00).

Response to Amendment

3. The following rejections, in paper number 13 (4/10/00), are withdrawn in light of applicants' amendments and arguments filed on 10/16/00 : under 35 U.S.C. 112, second paragraph, a) rejection of claims 1 and 3 pertaining to molecular weight determination, claims 1 and 26 pertaining to antibodies generated against SEQ ID NO:s:1, 3, 16, claim 12 as pertaining to a "variant"and "a core domain"; under 35 U.S.C. 112, first paragraph, rejection of claim 14; and under 35 U.S.C. 102, rejection of claim 12

Claim Rejection, 35 U.S.C. 112, second paragraph

4. Claims 1-16, 26-27 and 44-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, 13, 14, 26 and 48 are indefinite because it is not clear what activity is increased so as to allow the metes and bounds of the claims to be determined.

Claim 1, 13, 14, 26 and 48 are indefinite because it is not clear what must be combined with the monomer to form the "functional tetrameric form" and what function the tetrameric form has, so as to allow the metes and bounds of the claims to be determined.

Claims 2 and 3 are indefinite because it is not clear what is a mSlo3 or hSlo3 encoded polypeptide. Since the names mSlo3 or hSlo3 are not an art accepted description of the proteins they do not sufficiently describe said proteins. Applicant argues that page 13, line 31 to page 14, line and page 14, lines 16-25 define mSlo3 or hSlo3. Applicants arguments have been fully considered but not found persuasive because, by applicants definition, any nucleic acid that binds to the nucleic acids of SEQ ID Nos: 2, 17 and 19, under undefined hybridization conditions, can be considered Mlo3 or hSlo3, and therefore the use of the names mSlo3 or hSlo3 do not provide any structural and functional limitations, so as to allow the metes and bounds of the claim to be determined. It is suggested mSlo3 or hSlo3 be identified by SEQ ID NO:.

Claims 6-7 and 13 remains rejected because, although, some of the hybridization conditions are now disclosed ("end" wash conditions), the beginning "moderate stringency hybridization conditions" are still not specified. The metes and bounds of the group of sequences that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed (beginning and end). Since the hybridization and wash conditions dictate which DNA sequences remain specifically bound to the DNA of SEQ ID NO:2, 4, 17 and 19 the metes and bounds of the claims cannot be determined without the disclosure of said conditions.

Claim 45 is indefinite because the method of determining the molecular weight has not been identified. A value for the molecular weight is entirely dependent upon the method by which it is determined and differs with different methods (e.g. denaturing gel, native gel, calculated from amino

acid sequence, gel filtration etc.). Recitation of a molecular value without reference to the method by which it was measured is indefinite.

Claims 10-11 remain indefinite because "stringent hybridization conditions" are not specified. Applicant argues that "stringent hybridization conditions" refers to standard conditions. Applicants arguments have been fully considered but not found persuasive because The metes and bounds of the group of sequences that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed. Since the hybridization and wash conditions dictate which DNA sequences remain specifically bound to the DNA of SEQ ID NO:8-15 the metes and bounds of the claims cannot be determined without the disclosure of said conditions.

Claims 4-5, 9, 15-16, 27 and 46-47 are indefinite for depending on a base claim or intermediate claim and fail to resolve the issues raised above.

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-4, 7, 9-14, 26-2745-48 , as pertaining to the nucleic acid disclosed in SEQ ID NO:4, encoding the polypeptide of SEQ ID NO:3, and sequences that hybridize to the nucleic acid of SEQ ID NO:4 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

A "specific utility" is a utility that is specific to the subject matter claimed, as opposed to a "general utility" that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention.

Applicant has asserted utilities for the specifically claimed invention of claims 1-4, 7, 9-14, 26-2745-48

The claims are directed to isolated polynucleotide comprising a sequence encoding the polypeptide of: a) SEQ ID NOs: 1, 3, 16 and 18 or other proteins which have specific functional features associated with the claimed pH sensitive potassium channel.

It appears from the specification that the nucleic acid of SEQ ID NOs: 2, 17 and 19 encode full length monomer of a pH sensitive potassium channel, the monomer having a unit conductance

of approximately 80-120 pS when the monomer is in a functional tetramaric form, capable of transporting potassium ions, having increased potassium ion transporting activity above an intracellular pH of 7.1, specifically binding to polyclonal antibodies generated against a polypeptide comprising an amino acid sequence of SEQ ID NO:1, 16 or 18 (encoded by the DNA of SEQ ID NOS:2, 17 and 19). The specification further provides a partial sequence for a nucleic acid (SEQ ID NO:4) encoding the partial sequence of the polypeptide of SEQ ID NO:3. The specification nor prior art disclose if said partial nucleic acid encodes a functional protein, nor the activity associated with said protein.

The applicant has mentioned general functional activities which may be applicable to known pH sensitive potassium channel proteins but not disclosed any specific activity associated with the specific protein of SEQ ID NO:4 of instant invention. In light of the specification the skilled artisan can speculate that the polypeptide of SEQ ID NO:3 and nucleic acid that hybridize to the nucleic acid of SEQ ID NO:4 belonging to the pH sensitive potassium channel proteins. However, apart from the disclosure of SEQ ID NOS:1-4 and 16-18 no other disclosure is provided within the instant specification on what the structural and functional features the protein of SEQ ID NO:3 possesses, nor are any disease states disclosed that are directly related to its dysfunction.

The utilities asserted by Applicant are not specific or substantial. Since no specific function of the polypeptide of instant invention is known, and the hypothesized function is based entirely on conjecture from homologous polypeptides, the asserted utilities are not specific to instant polypeptide, but rather are based on family attributes. Neither the specification nor the art of record

disclose the nucleic acids of SEQ ID NO:4 encoding the proteins of SEQ ID NO:3 and 4, respectively, useful to identify drugs that affect said proteins and modulate their activity. Similarly, neither the specification nor the art of record disclose any instances where disorders can be effected by interfering with the activity using the polypeptide of SEQ ID NO:3. Thus the corresponding asserted utilities are essentially methods of using polynucleotide of SEQ ID NO:4 to identify other nucleic acids that hybridize to said polynucleotide, or to isolate disease states associated with polypeptide disfunction, and as targets for drug discovery. Therefore the asserted utilities are essentially methods of isolating, testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating, isolating or testing for compounds that interact with the polypeptide of SEQ ID NO:3 or polynucleotide of SEQ ID NO:4, which may be implicated in an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed polynucleotide of SEQ ID NO:4 or nucleic acids that hybridize to said polynucleotide, further experimentation is necessary to attribute a utility to the claimed polypeptides and polynucleotide. See Brenner v. Manson, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Accordingly, the instant

specification provides insufficient guidance on "how to use" polynucleotide of SEQ ID NO:3 of instant invention. Likewise, the instant specification provides insufficient guidance on "how to use" vector containing nucleic acid of claim 1 and cell containing said vector.

Claim Rejection, 35 U.S.C. 112, first paragraph

6. Claims 1-3, 6-7, 9-14, 26-27 and 45-48 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a polypeptide monomer of a pH sensitive potassium channel, the monomer having a unit conductance of approximately 80-120 pS when the monomer is in a functional tetramaric form capable of transporting potassium ions, having increased potassium ion transporting activity above an intracellular pH of 7.1, specifically binding to polyclonal antibodies which are specific against a polypeptide consisting of the amino acid sequence of SEQ ID NO:1, 16 or 18 (encoded by the isolated nucleic acid of SEQ ID NOS:2, 17 and 19), wherein said isolated nucleic acid hybridizes to the nucleic acid of SEQ ID NOs:2, 17 and 19 under moderate stringency hybridization conditions of 40% formamide, 1M NaCl and 1% SDS at 37°C and wash in 1X SSC at 45 °C, or where said isolated nucleic acid is amplified by primers of SEQ ID NOs:8-15 under the stringent hybridization conditions of 50% formamide, 5xSSC and 1% SDS at 42°C and wash in 0.2X SSC and 0.1% SDS at 65 °C, does not reasonably provide enablement for nucleic acid hybridizing under unspecified conditions, nucleic acid hybridizing to the nucleic acid of SEQ ID NO:4 or to DNA encoding protein which bind to sequences not specific to the protein of SEQ ID NOs: 1, 16 and 18. The, specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Hybridization conditions have not been provided. Therefore the hybridization conditions recited in the claim do not constitute a meaningful structural limitation. Since the hybridization and wash conditions dictate which nucleic acid sequences remain specifically bound to the nucleic acid of SEQ ID NOs:2, 4, 8-15, 17 and 19, the metes and bounds of the claims cannot be determined without the disclosure of said conditions. Due to the large quantity of experimentation necessary to identify the polypeptides with the structural and functional features of instant invention without any disclosure of the hybridization or wash conditions, the unpredictability of isolating proteins unrelated to SEQ ID NO:s 1, 16 and 18, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope. Further, since SEQ ID NO:4 encodes a partial sequence for a polypeptide of SEQ ID NO:3, it not clear if said polypeptide is an ion channel, undue experimentation would be required of the skilled artisan to use SEQ ID NO:4 to predictably isolate the polypeptide of instant invention. Further, the claims encompass nucleic acids which encode proteins which specifically bind to polyclonal antibodies generated against a polypeptide comprising the amino acid sequence of SEQ ID NOs:1, 3, 16 or 18. The proteins that bind to polyclonal antibodies generated against a polypeptide comprising the amino acid sequence of SEQ ID NO:1, 3, 16 or 18 may be unrelated to those of instant invention because they may comprise epitopes not contained in the polypeptide of SEQ ID NOs: 1, 3, 16 or 18 e.g. due to chimeric constructs. Therefore the claims due not provide a structural limitation commensurate in scope of the claimed

invention because an infinite number of nucleic acids is encompassed by nucleic acids encoding proteins which bind to sequences comprising the afore mentioned proteins. Therefore due to the unpredictability of isolating proteins related to SEQ ID NO:s 1, 16 and 18 with the functional properties listed above, without a defined structural limitation, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

Claim Rejection, 35 U.S.C. 112, first paragraph

7. Claims 1-4, 7, 9-14, 26-27, 45-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompass the polynucleotide:

a) encoding the polypeptide comprising SEQ ID NO:3

b) that hybridize to the nucleic acid SEQ ID NO:3

c) amplified by primers of SEQ ID NO:8-15

d) encoding fragments of SEQ ID NOS:1, 3, 16 and 18 which are at least 25 contiguous amino acids.

e) encoding a polypeptide specifically binding to polyclonal antibodies generated against a polypeptide **comprising** an amino acid sequence of SEQ ID NO:1, 3, 16 or 18.

The claims are further directed to vector and cell comprising the above disclosed polynucleotide.

The claims encompass polynucleotide encoding the polypeptide of e) above, said polypeptide may be unrelated to those of instant invention because the polypeptide may comprise epitopes not contained in the polypeptide of SEQ ID NOs: 1, 3, 16 or 18, e.g.. due to chimeric constructs being used to generate antibodies. Therefore, the claims containing antibodies due not provide a defined structural limitation and encompasses an infinite number of possible nucleic acids which encompasses a substantial variety of subgenera including full-length genes, nucleic acids encoding chimeric proteins or fusion proteins and variants. The claims, as written, also encompass polynucleotide of SEQ ID NO:4 which vary substantially in length and also in nucleotide composition. The instant disclosure of a partial sequence of the polynucleotide of SEQ ID NOs:4 does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes, nucleic acids encoding chimeric proteins or fusion proteins and variants. Also the nucleic acid of d) encoding fragments of SEQ ID NOS:1, 3, 16 and 18 which are at least 25 contiguous amino acids provides no guidance as to which 25 contiguous aminos contain a defined functional feature. The same is true for variants encompassed by nucleic acids encoding polypeptide having more than 60% identity to polypeptide comprising amino acids 35-641 of SEQ ID NO:1. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the

genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotide of SEQ ID NO:4, or those of a polypeptide specifically binding to polyclonal antibodies generated against a polypeptide comprising an amino acid sequence of SEQ ID NO:1, 3, 16 or 18.. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. The specification proposes to discover other members of the genus by using techniques involving probes, primers, hybridization and antibodies. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotide of SEQ ID NO:4 or those encoding a polypeptide specifically binding to polyclonal antibodies generated against a polypeptide comprising an amino acid sequence of SEQ ID NO:1, 3, 16 or 18. No identifying characteristic or property of the afore mentioned polynucleotide is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific nucleotide sequences with no disclosed function, is insufficient to describe the

genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Accordingly, the specification does not provide a written description of the polynucleotide comprising a)-e) (full-length genes, nucleic acids encoding chimeric proteins or fusion proteins and variants, disclosed above), and further the claims do not provide written description of cells comprising non-native polynucleotide of SEQ ID NO:4 and the polynucleotide comprising a)-e).

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
December 29, 2000

YVONNE EYLER, PH.D
PRIMARY EXAMINER